UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,274	12/27/2001	C. Michael Philbrook	5052	8081

24536 7590 06/30/2003

GENZYME CORPORATION
LEGAL DEPARTMENT
15 PLEASANT ST CONNECTOR
FRAMINGHAM, MA 01701-9322

EXAMINER
BENNETT, RACHEL M

ART UNIT	PAPER NUMBER
1615	12

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/033,274	Applicant(s) PHILBROOK ET AL.	
	Examin r Rachel M. Bennett	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 27-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6&8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 18-26 in Paper No. 11 is acknowledged.

Specification

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 18-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney et al. (US 5900245) and further in view of Levy et al. (US5387419).

Applicants claim a solution comprising biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form a tissue adhesive hydrogel degrading in a period of less than one month after application to the tissue and an anti-arrhythmic agent in a dosage effective to lengthen arterial effective refractory period.

Sawhney et al. disclose a drug delivery system which is highly adherent to the surface to which it is applied. The polymerized compliant coating is biodegradable and biocompatible and can be designed with selected properties of compliancy and elasticity for different surgical and therapeutic applications. See abstract. A two step process can be used to form polymers, especially bioabsorbable hydrogels on tissue. In the first step the tissue is treated with an initiator or a part of an initiator system for the polymerization of olefinic or other functional monomers, optionally with monomer in the priming solution. This provides an activated tissue surface. In the second step, monomer(s) and, if appropriate, the remainder of an initiator system, are together placed in contact with the activated tissue, resulting in polymerization on the tissue. See col. 6 lines 15-26. Monomers are disclosed in cols. 7-9. Surfaces to be treated include the pericardium. Active agents are disclosed in col. 12. In many applications, such as tissue sealing, the viscosity of the precursor materials can be tailored to obtain optimal coatings. The optimal viscosity will depend on the site of application and the nature of the condition which is to be alleviated by the application of the material. See col. 17, lines 24-38. Known viscosity modifying agents include dextran and polyvinylpyrrolidone. A convenient way to package the materials is in three vials (or prefilled syringes), one of which contains concentrated initiator for priming, the second of the which contains reconstitution fluid, and the third containing dry or lypholized monomer. See col. 17, lines 39-55. Sawhney does not specifically disclose the biologically active ingredient to be an anti-arrhythmic agent such as amiodarone.

Levy et al. disclose a system for controlled release, sit specific delivery of therapeutic agents, particularly myocardial agents such as antiarrhythmic agents, comprising a biocompatible polymeric matrix with an incorporated therapeutic agent for direct placement a the epicardium

(the inner par the of the pericardium that closely envelops the heart). Advantageously, the dosage form can be fabricated in such as manner as to tailor the release characteristics as required by the nature of the physical condition desired to be treated. See abstract. Amiodarone is highly effective antiarrhythmic agent which is frequently associated with severe side effects. It efficacy when utilized in a controlled release dosage form demonstrates that the transmyocaridal route of administration may be the safest and most effective manner of delivering this drug.

Absent unexpected results, it is the position of the examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Sawhney by substituting the antiarrhythmic, amiodarone as taught by Levy, for the active agent because of the expectation of delivery a highly effective antiarrhythmic to the pericardium in a safe and effective manner as taught by Levy. The expected result would be a solution comprising biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form a tissue adhesive hydrogel comprising amiodarone.

5. Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perdue Research Foundation (WO 02/16442 A2).

Applicants claim a solution comprising biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form a tissue adhesive hydrogel degrading in a period of less than one month after application to the tissue and an anti-arrhythmic agent in a dosage effective to lengthen arterial effective refractory period.

Perdue Research Foundation discloses a cross-linked hydrogel composition in the form of substantially uniform microparticles and method of preparation therefor. The hydrogel composition comprises a crosslinked polymer formed by free radical polymerization of olefin

monomers comprising a C_3-C_6 unsaturated carboxylic acid and a water dispersible polyolefin crosslinking agent. The olefin monomers may further comprise a polyaklyleneglycol monoacrylate or monometheacrylate. See abstract. The release rate of the active increases with decreasing amount of PEGDMA. Representative drugs include antiarrhythmics. See page 8. The particulate hydrogel can be used for administration to a patient and can be suspended or dispersed in a liquid carrier. See page 10. Perdue Research Foundation does not disclose the hydrogel to degrade in a period of less than one month after application.

Absent unexpected results, it is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Perdue Research Foundation by adjusting the amount of PEGDMA because of the expectation of determining the desired release rate as taught by Perdue Research Foundation. The expected result would be a solution comprising biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable degrading in a period of less than one month after application to the tissue and an anti-arrhythmic agent in a dosage effective to lengthen arterial effective refractory period.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

rmb
June 26, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600